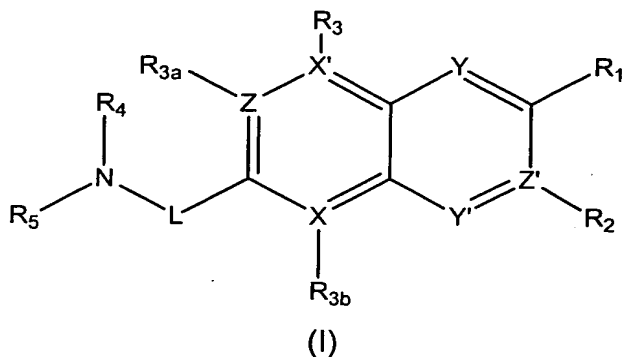


WHAT IS CLAIMED IS:

1. A compound of the formula:



or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein:

Y, and Y' are each independently selected from the group consisting of CH, CF, and N;

X, X', Z, and Z' are each independently C or N;

one of R₁ and R₂ is selected from the group consisting of halogen, cyano, and L₂R₆;

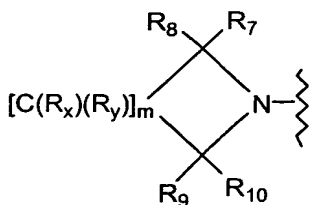
the other of R₁ and R₂ is selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, cycloalkyl, halogen, cyano, and thioalkoxy, provided that R₂ is absent when Z' is N;

R₃ is absent when X' is N or R₃ is selected from the group consisting of hydrogen, alkyl, alkoxy, halogen, cyano, and thioalkoxy;

R_{3a} is absent when Z is N or R_{3a} is selected from the group consisting of hydrogen, methyl, alkoxy, halogen, and cyano;

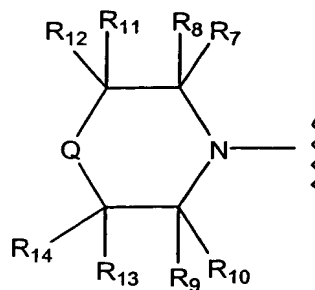
R_{3b} is absent when X is N or R_{3b} is selected from the group consisting of hydrogen, alkyl, alkoxy, halogen, hydroxy, cyano, and thioalkoxy;

R₄ and R₅ are each independently selected from the group consisting of alkyl, haloalkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, and (NR_AR_B)alkyl, or R₄ and R₅ taken together with the nitrogen atom to which each is attached form a non-aromatic ring of the formula:



(a)

or



(b)

;

R_6 is selected from the group consisting of aryl, heteroaryl, heterocycle, and cycloalkyl;

R_7 , R_8 , R_9 , and R_{10} at each occurrence are each independently selected from the group consisting of hydrogen, hydroxyalkyl, fluoroalkyl, and alkyl; or one of the pair R_7 and R_8 or the pair R_9 and R_{10} is taken together to form a C_3-C_6 ring, wherein 0, 1, or 2 heteroatoms selected from O, N, or S replace a carbon atom in the ring;

R_{11} , R_{12} , R_{13} , and R_{14} are each independently selected from the group consisting of hydrogen, hydroxy, hydroxyalkyl, alkyl, and fluoro;

Q is selected from the group consisting of a bond, O, S, and NR_{15} ;

L is $-[C(R_{16})(R_{17})]_n-$ or $-[C(R_{16})(R_{17})]_pO-$;

L_2 is selected from the group consisting of a bond, $-O-$, $-C(=O)-$, $-S-$, $-[C(R_{18})(R_{19})]_q-$, $-O-[C(R_{18})(R_{19})]_q-$, $-NH-$ and $-N(alkyl)-$;

R_{15} is selected from the group consisting of hydrogen, alkyl, acyl, amido, and formyl;

R_{16} and R_{17} at each occurrence are independently selected from the group consisting of hydrogen, alkyl, alkoxy, and fluoro;

R_{18} and R_{19} at each occurrence are each independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkoxy, and fluoro;

R_x and R_y at each occurrence are independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkoxy, alkylamino, dialkylamino, and fluoro, or one of R_x or R_y represents a covalent bond when taken together with R_x or R_y on an adjacent carbon atom such that a double bond is represented between the adjacent carbon atoms;

m is an integer from 1 to 5;

n is an integer from 1 to 6;

p is an integer from 2 to 6; and

q is an integer from 1 to 4;

wherein 0, 1, or 2 of X, X', Y, Y', Z, and Z' can be nitrogen; provided that R₃

5 is absent when X' is N; R_{3a} is absent when Z is N; R₂ is absent when Z' is N, and R_{3b} is absent when X is N.

2. The compound of claim 1, wherein R₁ is bromo, cyano, or L₂R₆.

10 3. The compound of claim 1, wherein R₁ is L₂R₆, L₂ is -CH(OH)-, -C(=O)-, or a bond, and R₆ is aryl, heteroaryl, heterocycle, or cycloalkyl.

4. The compound of claim 1, wherein R₁ is L₂R₆, L₂ is a bond, and R₆ is aryl wherein the aryl is phenyl substituted with 0, 1, or 2 substituents selected from the
15 group consisting of cyano, halogen, -NR_AR_B, alkoxy, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, cycloalkylcarbonyl, alkylsulfonyl, haloalkyl, and thioalkoxy.

5. The compound of claim 1, wherein R₁ is L₂R₆, L₂ is a bond, and R₆ is selected from the group consisting of furyl, imidazolyl, isothiazolyl, isoxazolyl,
20 oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridazinonyl, pyridinonyl, pyridinyl, pyrimidinyl, pyrrolyl, tetrazolyl, thiadiazolyl, thiazolyl, thienyl, triazinyl, and triazolyl, substituted with 0, 1, 2, or 3 substituents selected from the group consisting of -NR_AR_B, halogen, alkyl, cyano, alkoxyimino, alkoxycarbonyl, (NR_AR_B)carbonyl, alkylcarbonyl, haloalkyl, and alkoxy.

25 6. The compound of claim 1, wherein R₁ is L₂R₆, L₂ is a bond, and R₆ is selected from the group consisting of azepanyl, azetidiny, aziridinyl, azocanyl, dihydrothiazolyl, morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, pyrrolinyl, thiomorpholinyl, tetrahydropyridinyl, tetrahydrofuryl, and tetrahydropyranyl.

30 7. The compound of claim 1, wherein R₄ and R₅ are each independently selected from methyl, ethyl, and propyl.

8. The compound of claim 1, wherein R_4 and R_5 taken together with the nitrogen atom to which each is attached form a 4- to 8-membered non-aromatic ring represented by formula (a).

5 9. The compound of claim 8, wherein the 4- to 8-membered non-aromatic ring is selected from the group consisting of azetidiny, azepanyl, azepiny, pyrrolidiny, pyrroliny, piperidiny, piperaziny, and tetrahydropyridiny, substituted with 0, 1, or 2 substituents selected from the group consisting of alkyl, hydroxyalkyl, fluoroalkyl, and $-NR_A R_B$.

10 10. The compound of claim 8, wherein at least one substituent represented by R_7 , R_8 , R_9 , and R_{10} is selected from the group consisting of alkyl, halogen, fluoroalkyl, and hydroxyalkyl or at least one substituent represented by R_x or R_y is selected from the group consisting of hydrogen, hydroxy, and fluoro.

15 11. The compound of claim 8, wherein the 4- to 8-membered non-aromatic ring is selected from the group consisting of methylpyrrolidiny, ethylpyrrolidiny, dimethylaminopyrrolidiny, isopropylpyrrolidiny, isobutylpyrrolidiny, hydroxymethylpyrrolidiny, and fluoromethylpyrrolidiny.

20 12. The compound of claim 1, wherein R_4 and R_5 taken together with the nitrogen atom to which each is attached form morpholiny or thiomorpholiny.

25 13. The compound of claim 1, wherein at least one substituent represented by R_7 , R_8 , R_9 , and R_{10} is hydroxyalkyl, fluoroalkyl, or alkyl.

14. The compound of claim 1, wherein at least one substituent represented by R_7 , R_8 , R_9 , and R_{10} is methyl, ethyl, fluoromethyl, or hydroxymethyl.

30 15. The compound of claim 1, wherein one substituent represented by R_7 , R_8 , R_9 , and R_{10} is alkyl and the other three substituents are hydrogen.

16. The compound of claim 1, wherein R_{11} , R_{12} , R_{13} , and R_{14} are each hydrogen.

17. The compound of claim 1, wherein R_{11} and R_{12} each are hydrogen, and R_{13} and R_{14} are each independently selected from the group consisting of hydrogen and alkyl.

18. The compound of claim 1, wherein R_{15} is selected from the group consisting of hydrogen, alkyl, amido, and formyl.

19. The compound of claim 1, wherein R_{16} and R_{17} are hydrogen.

20. The compound of claim 1, wherein R_{18} and R_{19} are hydrogen.

21. The compound of claim 1, wherein m is 2 or 3.

22. The compound of claim 1, wherein n is 2 or 3.

23. The compound of claim 1, wherein p is 2.

24. The compound of claim 1, wherein q is 1.

25. The compound of claim 1, wherein
Y and Y' are CH;
X, X', Z, and Z' are C; and
 R_2 , R_3 , R_{3a} , and R_{3b} are hydrogen.

26. The compound of claim 1, wherein
Y and Y' are CH;
X, X', and Z are C;
 R_3 , R_{3a} , and R_{3b} are hydrogen;
Z' is N; and
 R_2 is absent.

27. The compound of claim 1, wherein

Y and Y' are CH;

X', Z', and Z are C;

R₂, R₃, and R_{3a} are hydrogen;

X is N; and

R_{3b} is absent.

28. The compound of claim 1, wherein

Y and Y' are CH;

X, X', and Z' are C;

R₂, R₃, and R_{3b} are hydrogen;

Z is N; and

R_{3a} is absent.

29. The compound of claim 1, wherein

Y is CH;

X, X', Z, and Z' are C;

R₂, R₃, R_{3a}, and R_{3b} are hydrogen; and

Y' is N.

30. The compound of claim 1, wherein

Y and Y' are CH;

X and Z' are C;

R₂ and R_{3b} are hydrogen;

X' is N;

Z is N; and

R₃ and R_{3a} are absent.

31. The compound of claim 1, wherein

X, X', Z, and Z' are C;

R₂, R₃, R_{3a}, and R_{3b} are hydrogen;

Y is N; and

Y' is N.

32. The compound of claim 1, wherein

Y' is CH;

X, X', and Z are C;

R₃, R_{3a}, and R_{3b} are hydrogen;

Y is N;

Z' is N; and

R₂ is absent.

33. The compound of claim 1, wherein

Y' is CH;

X, Z, and Z' are C;

R₂, R_{3a}, and R_{3b} are hydrogen;

Y is N;

X' is N; and

R₃ is absent.

34. The compound of claim 1, wherein

Y' is CH;

X, X', and Z' are C;

R₂, R₃, and R_{3b} are hydrogen;

Y is N;

Z is N; and

R_{3a} is absent.

35. The compound of claim 1, wherein

Y is CH;

X, X', and Z are C;

R₃, R_{3a}, and R_{3b} are hydrogen;

Y' is N;

Z' is N; and

R₂ is absent.

36. The compound of claim 1, wherein

Y and Y' are CH;

Z' and Z are C;

5 R₂ and R_{3a} are hydrogen;

X' is N;

X is N; and

R₃ and R_{3b} are absent.

10 37. The compound of claim 1, wherein

Y' is CH;

X, X', Z and Z' are C;

R₂, R₃, R_{3a}, and R_{3b} are hydrogen; and

Y is N.

15

38. The compound of claim 1, wherein

Y and Y' are CH;

X' and Z' are C;

R₂ and R₃ are hydrogen;

20 X is N;

Z is N; and

R_{3a} and R_{3b} are absent.

39. The compound of claim 1, wherein

25 Y is CH;

X, Z', and Z are C;

R₂, R_{3a}, and R_{3b} are hydrogen;

Y' is N;

X' is N; and

30 R₃ is absent.

40. The compound of claim 1, wherein:

R₁ is L₂R₆ wherein L₂ is a bond and R₆ is heteroaryl or heterocycle;

R₂, R₃, R_{3a}, and R_{3b} are hydrogen;

L is -[C(R₁₆)(R₁₇)]_n-;

n is 2;

R₁₆ and R₁₇ at each occurrence are hydrogen;

5 R₄ and R₅ are taken together to form a methylpyrrolidinyl ring of formula (a), wherein one of R₇, R₈, R₉, and R₁₀ is methyl and the remaining three substituents are hydrogen;

Y and Y' are CH; and

X, X', Z, and Z' are C.

10 41. The compound of claim 40, wherein R₁ is a heteroaryl group selected from 2H-pyridazin-3-one-2-yl.

42. The compound of claim 1, selected from the group consisting of
15 4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;
(2R)-1-[2-(6-bromo-2-naphthyl)ethyl]-2-methylpyrrolidine;
1-[3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)phenyl]ethanone;
2-[3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)phenyl]-2-
propanol;

20 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthonitrile;
4-(6-{[(2R)-2-methyl-1-pyrrolidinyl]methyl}-2-naphthyl)benzonitrile;
3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;
4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyridine;
3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyridine;
25 (3-fluorophenyl)(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-
naphthyl)methanol;
3,5-dimethyl-4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-
naphthyl)isoxazole;

30 4-(6-{2-[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;
4-(6-{2-[(3R)-3-hydroxy-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;
4-{6-[2-(2-isobutyl-1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;
4-{6-[2-(2-isopropyl-1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;
4-(6-{2-[(3R)-3-(dimethylamino)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;

4-{6-[2-(diethylamino)ethyl]-2-naphthyl}benzonitrile;
 4-{6-[2-(dimethylamino)ethyl]-2-naphthyl}benzonitrile;
 4-(6-{2-[ethyl(isopropyl)amino]ethyl}-2-naphthyl)benzonitrile;
 4-(6-{2-[tert-butyl(methyl)amino]ethyl}-2-naphthyl)benzonitrile;
 5 4-(6-{2-[(2S)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;
 4-(6-{2-[(2R)-2-methyl-1-piperidinyl]ethyl}-2-naphthyl)benzonitrile;
 4-{6-[2-(2,5-dihydro-1*H*-pyrrol-1-yl)ethyl]-2-naphthyl}benzonitrile;
 4-(6-{2-[methyl(propyl)amino]ethyl}-2-naphthyl)benzonitrile;
 4-(6-{2-[(2-hydroxyethyl)(methyl)amino]ethyl}-2-naphthyl)benzonitrile;
 10 5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyrimidine;
 4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)morpholine;
 2-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)-1,3-thiazole;
 4-(6-{2-[(2S)-2-(fluoromethyl)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;
 (3-fluorophenyl)(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-
 15 naphthyl)methanone;
 2-(6-{2-[(2R)-2-methyl-1-pyrrolidin-1-yl]-ethyl}-2-naphthalen-2-yl)-2*H*-
 pyridazin-3-one;
 2-methoxy-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)pyridine;
 4-(6-{2-[(2R)-2-(hydroxymethyl)-1-pyrrolidinyl]ethyl}-2-naphthyl)benzonitrile;
 20 4-{6-[2-(2-methyl-1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;
 4-{6-[2-(1-pyrrolidinyl)ethyl]-2-naphthyl}benzonitrile;
 4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-naphthyl)thiomorpholine;
 1-{2-[(6-bromo-2-naphthyl)oxy]ethyl}pyrrolidine;
 3-{6-[2-(1-pyrrolidinyl)ethoxy]-2-naphthyl}benzonitrile;
 25 3-{6-[2-(1-pyrrolidinyl)ethoxy]-2-naphthyl}pyridine;
 3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethoxy}-2-naphthyl)benzonitrile;
 3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethoxy}-2-naphthyl)pyridine;
 4-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)benzonitrile;
 6-(4-fluorophenyl)-2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;
 30 3-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)benzonitrile;
 1-[3-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)phenyl]ethanone;
 6-(4-methoxyphenyl)-2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;

2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-[4-(trifluoromethyl)phenyl]quinoline;

2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-[4-(methylsulfonyl)phenyl]quinoline;

5 6-(3,5-difluorophenyl)-2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;
6-(3-fluorophenyl)(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinolinyl)methanone;

2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-(3-pyridinyl)quinoline;

4-(3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-7-isoquinolinyl)benzonitrile;

10 3-(3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-7-isoquinolinyl)benzonitrile;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(3-pyridinyl)quinoline;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-pyridinyl)quinoline;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(2-pyridinyl)quinoline;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(1,3-thiazol-2-yl)quinoline;

15 2-(2,4-dimethyl-1,3-thiazol-5-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(2-pyrazinyl)quinoline;

1-[6-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-2-pyridinyl]ethanone;

20 4-(2-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinoxaliny)benzonitrile;

4-(3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-6-quinoxaliny)benzonitrile;

7-(2,6-difluoro-3-pyridinyl)-3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}isoquinoline;

3-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-7-(3-pyridinyl)isoquinoline;

25 3-(benzyloxy)-2-methyl-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;

2-cyclopropyl-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;

4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)benzonitrile;

2,6-dimethyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)nicotinonitrile;

30 2-(3-methyl-2-pyrazinyl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;

ethyl 5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-3-isoxazolecarboxylate;

5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-2-thiophenecarbonitrile;

ethyl 5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-2-thiophenecarboximidoate;

5 2-(2,4-dimethyl-1,3-oxazol-5-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}quinoline;

ethyl 3-methyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-quinolinyl)-4-isoxazolecarboxylate;

4-(7-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-3-isoquinolinyl)benzonitrile;

10 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-methoxyphenyl)quinoxaline;

7-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-methoxyphenyl)quinoxaline;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-phenylquinoxaline;

7-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-phenylquinoxaline;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(3-pyridinyl)quinazoline;

15 6-methyl-2-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-2H-pyridazin-3-one;

5-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrimidine-2-carbonitrile;

20 1-{6-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-1H-pyridin-2-one;

5-{6-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-nicotinonitrile;

4-methyl-1-{6-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-1H-pyridin-2-one;

2-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrazine;

25 2-{6-[2-((2R)-2-methyl-2,5-dihydro-pyrrol-1-yl)-ethyl]-naphthalen-2-yl}-2H-pyridazin-3-one;

4-(6-{2-[(2-dimethylamino-ethyl)-methyl-amino]-ethyl}-naphthalen-2-yl)-benzonitrile;

4-{6-[2-(4-methyl-piperazin-1-yl)-ethyl]-naphthalen-2-yl}-benzonitrile;

30 2-(2,5-dimethyl-furan-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;

6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(4-methylsulfanyl-phenyl)-quinoline;

2-(6-methyl-pyridin-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;
 2-(1,3-dimethyl-1*H*-pyrazol-4-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-
 quinoline;
 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-thiophen-3-yl-quinoline;
 5 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-pyrimidin-5-yl-quinoline;
 2-(2,6-dimethyl-pyridin-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-
 quinoline;
 1-[2,6-dimethyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-
 pyridin-3-yl]-ethanone.;
 10 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(2*H*-pyrazol-3-yl)-quinoline;
 2-(3-bromo-isoxazol-5-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;
 2-(6-chloro-pyridin-3-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;
 2-(3,5-dimethyl-thiophen-2-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-
 quinoline;
 15 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-thiophen-2-yl-quinoline;
 2-furan-3-yl-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinoline;
 2-(4,5-dihydro-thiazol-2-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-
 quinoline;
 1-[4-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-phenyl]-
 20 ethanone;
 3-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-2-trifluoromethyl-
 pyridin-4-ol;
 2-(3,5-dimethyl-1*H*-pyrazol-4-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-
 quinoline;
 25 6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-2-(1*H*-pyrazol-4-yl)-quinoline;
 2,6-dimethyl-5-(6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-quinolin-2-yl)-
 nicotinamide;
 2-[2-(2R-methyl-pyrrolidin-1-yl)-ethyl]-6-pyridin-4-yl-quinoline;
 6-(6-methoxy-pyridin-3-yl)-2-[2-(2R-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;
 30 6-(2,6-difluoro-pyridin-3-yl)-2-[2-(2R-methyl-pyrrolidin-1-yl)-ethyl]-
 quinoline;
 6-(6-chloro-pyridin-3-yl)-2-[2-(2R-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;

6-(2,6-dichloro-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-
quinoline;

2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-6-pyrazin-2-yl-quinoline;

2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-6-pyrimidin-5-yl-quinoline;

5 6-(2,4-dimethoxy-pyrimidin-5-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-
quinoline;

dimethyl-(4-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-phenyl)-
amine;

10 1-(4-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-phenyl)-
ethanone;

6-(4-chloro-phenyl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;

6-(2,6-dimethyl-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-
quinoline;

6-(5-methoxy-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;

15 6-(3,5-dimethyl-isoxazol-4-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-
quinoline;

4-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-benzoic acid methyl
ester;

20 2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-6-(4-methylsulfanyl-phenyl)-
quinoline;

6-(6-fluoro-pyridin-3-yl)-2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinoline;

5-{2-[2-(2(R)-methyl-pyrrolidin-1-yl)-ethyl]-quinolin-6-yl}-nicotinonitrile;

2,4-dimethoxy-5-{6-[2-((2R)-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-
pyrimidine;

25 2,6-difluoro-3-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-
pyridine;

cyclopropyl-(4-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-
phenyl)-methanone;

30 3-methoxy-6-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-
pyridazine;

4-{6-[2-(2-methyl-piperidin-1-yl)-ethyl]-naphthalen-2-yl}-benzonitrile;

4-{6-[2-((2R)-2-ethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-benzonitrile;

2-{6-[2-((2S)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

2-[6-((2R)-2-piperidin-1-yl-ethyl)-naphthalen-2-yl]-2*H*-pyridazin-3-one;

2-{6-[2-(tert-butyl-methyl-amino)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-

5 one;

2-[6-(2-diethylamino-ethyl)-naphthalen-2-yl]-2*H*-pyridazin-3-one;

2-[6-(2-morpholin-4-yl-ethyl)-naphthalen-2-yl]-2*H*-pyridazin-3-one;

2-{6-[2-(ethyl-methyl-amino)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

2-{6-[2-((2S)-2-fluoromethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-

10 pyridazin-3-one;

2-{6-[2-(2-hydroxymethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

2-{6-[2-((R)-2-ethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

15 2-[6-(2-azetidin-1-yl-ethyl)-naphthalen-2-yl]-2*H*-pyridazin-3-one;

2-{6-[2-((2S)-2-fluoromethyl-azetidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

2-{6-[2-((2S)-2-hydroxymethyl-azetidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

20 2-{6-[2-((2R,5R)-2,5-Dimethyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

2-{6-[2-((2R,6S)-2,6-dimethyl-piperidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

25 2-{6-[2-((R)-3-hydroxy-piperidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

2-{6-[2-((R)-2-methyl-piperidin-1-yl)-ethyl]-naphthalen-2-yl}-2*H*-pyridazin-3-one;

2,6-dimethyl-3-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyridine;

30 5-{6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-thiazole;

2-{6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrimidine;

3-chloro-6-{6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyridazine;

5-{6-[2-((R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyrimidin-2-ylamine;

2-methyl-5-{6-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-naphthalen-2-yl}-pyridine;

5 3-bromo-7-(2-pyrrolidin-1-yl-ethyl)-[1,5]naphthyridine;

3-bromo-7-[2-(2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-[1,5]naphthyridine;

3-bromo-7-(2-piperidin-1-yl-ethyl)-[1,5]naphthyridine;

3-(2,6-dimethyl-pyridin-3-yl)-7-[2-(2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-[1,5]naphthyridine;

10 3-(2,4-dimethoxy-pyrimidin-5-yl)-7-[2-(2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-[1,5]naphthyridine;

3-(2,6-dimethyl-pyridin-3-yl)-7-(2-pyrrolidin-1-yl-ethyl)-[1,5]naphthyridine;

3-(2,4-dimethoxy-pyrimidin-5-yl)-7-(2-pyrrolidin-1-yl-ethyl)-[1,5]naphthyridine;

15 3-(2,6-dimethyl-pyridin-3-yl)-7-(2-piperidin-1-yl-ethyl)-[1,5]naphthyridine;

3-(2,4-dimethoxy-pyrimidin-5-yl)-7-(2-piperidin-1-yl-ethyl)-

[1,5]naphthyridine;

3-[2-(2R)-methyl-pyrrolidin-1-yl)-ethyl]-7-pyridin-4-yl-isoquinoline;

7-(6-methoxy-pyridin-3-yl)-3-[2-(2R)-methyl-pyrrolidin-1-yl)-ethyl]-

20 isoquinoline;

3-[2-(2R)-methyl-pyrrolidin-1-yl)-ethyl]-7-pyrimidin-5-yl-isoquinoline;

7-(6-fluoro-pyridin-3-yl)-3-[2-(2R)-methyl-pyrrolidin-1-yl)-ethyl]-isoquinoline;

5-{3-[2-(2R)-methyl-pyrrolidin-1-yl)-ethyl]-isoquinolin-7-yl}-nicotinonitrile;

7-(3-chloro-pyridin-4-yl)-3-[2-(2R)-methyl-pyrrolidin-1-yl)-ethyl]-

25 isoquinoline;

7-bromo-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-4-ol;

4-{3-[2-(2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;

7-bromo-4-chloro-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;

4-{4-hydroxy-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-

30 benzonitrile;

4-{4-isopropoxy-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;

4-{3-[2-(4-methyl-piperazin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;

4-[3-(2-piperidin-1-yl-ethyl)-cinnolin-7-yl]-benzonitrile;
4-[3-(2-pyrrolidin-1-yl-ethyl)-cinnolin-7-yl]-benzonitrile;
4-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;
4-{3-[2-((2R)-2-hydroxymethyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-

5 benzonitrile;

4-[3-(2-morpholin-4-yl-ethyl)-cinnolin-7-yl]-benzonitrile;
4-{3-[2-(4-methyl-piperidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;
4-{3-[2-(ethyl-methyl-amino)-ethyl]-cinnolin-7-yl}-benzonitrile;
7-(2,6-dimethyl-pyridin-3-yl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-

10 cinnoline;

7-(2,4-dimethoxy-pyrimidin-5-yl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-
cinnoline;

7-(6-methoxy-pyridin-3-yl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-
cinnoline;

15 3-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-benzonitrile;
5-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-nicotinonitrile;
7-(4-fluoro-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;
2-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-pyrrole-1-
carboxylic acid tert-butyl ester;

20 (3-{3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnolin-7-yl}-phenyl)-
methanol;

7-(3,5-difluoro-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;

3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-7-thiophen-3-yl-cinnoline;

7-(4-chloro-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;

25 7-(4-ethoxy-phenyl)-3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-cinnoline;

3-[2-((2R)-2-methyl-pyrrolidin-1-yl)-ethyl]-7-(1*H*-pyrrol-2-yl)-cinnoline; and

2-(1,5-dimethyl-1*H*-pyrazol-4-yl)-6-{2-[(2R)-2-methyl-1-pyrrolidinyl]ethyl}-

quinoline.

30 43. The compound of claim 1, that is 2-(6-{2-[(2R)-2-methyl-1-pyrrolidin-1-yl]-
ethyl}-2-naphthalen-2-yl)-2*H*-pyridazin-3-one or 2-(6-{2-[(2R)-2-methyl-1-
pyrrolidinyl]ethyl}-2-naphthyl)-3(2*H*)-pyridazinone.

44. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

5 45. A method of selectively modulating the effects of histamine-3 receptors in a mammal comprising administering an effective amount of a compound of claim 1.

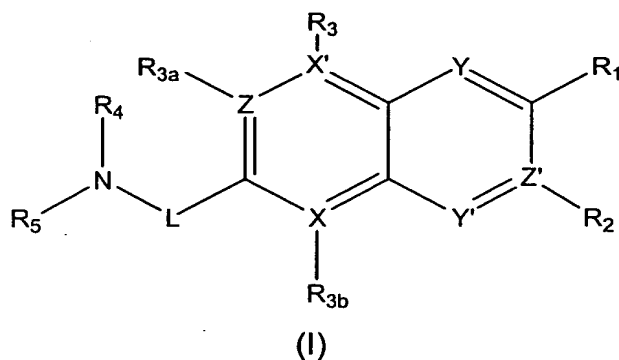
46. A method of treating a condition or disorder modulated by the histamine-3 receptors in a mammal comprising administering an effective amount of a
10 compound of claim 1.

47. The method according to claim 46, wherein the condition or disorder is selected from the group consisting of acute myocardial infarction, Alzheimer's disease, asthma, attention-deficit hyperactivity disorder, bipolar disorder, cognitive
15 dysfunction, cognitive deficits in psychiatric disorders, deficits of memory, deficits of learning, dementia, cutaneous carcinoma, drug abuse, diabetes, type II diabetes, depression, epilepsy, gastrointestinal disorders, inflammation, insulin resistance syndrome, jet lag, medullary thyroid carcinoma, melanoma, Meniere's disease, metabolic syndrome, mild cognitive impairment, migraine, mood and
20 attention alteration, motion sickness, narcolepsy, neurogenic inflammation, obesity, obsessive compulsive disorder, pain, Parkinson's disease, polycystic ovary syndrome, schizophrenia, cognitive deficits of schizophrenia, seizures, septic shock, Syndrome X, Tourette's syndrome, vertigo, and sleep disorders.

25 48. The method according to claim 46, wherein the condition or disorder affects the memory or cognition.

49. The method according to claim 46, wherein the condition or disorder is Alzheimer's disease, attention-deficit hyperactivity disorder, schizophrenia, or
30 cognitive deficits of schizophrenia.

50. A process for preparing a compound of formula (I):



or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, wherein:

R_1 is L_2R_6 wherein L_2 is a bond and R_6 is 3(2*H*)-pyridazinon-2-yl;

R_2 , R_3 , R_{3a} , and R_{3b} are hydrogen;

L is $-[C(R_{16})(R_{17})]_n-$;

n is 2;

R_{16} and R_{17} at each occurrence are hydrogen;

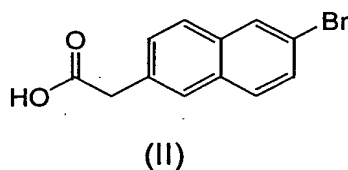
R_4 and R_5 are taken together to form a methylpyrrolidinyl ring of formula (a), wherein one of R_7 , R_8 , R_9 , and R_{10} is methyl and the remaining three substituents are hydrogen;

Y and Y' are CH; and

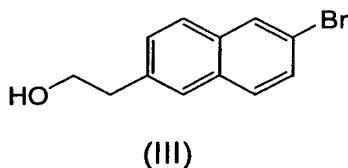
X , X' , Z , and Z' are C;

comprising the steps of:

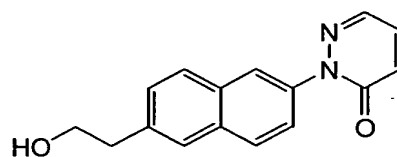
(a) providing a compound (II):



(b) reducing the compound (II) with BH_3 -THF to provide a compound (III):



(c) treating the compound of formula (III) with 3(2*H*)-pyridazinone, copper powder, and base to provide a compound (IV):



(IV)

(d) activating the hydroxy group of compound (IV); and reacting the resulting compound with methylpyrrolidine to provide a compound of formula (I).